Licensable Technologies

Protein Solubility and Folding Reporter Portfolio

Applications:

- Research and study of small molecules
- Biotech and pharmaceutical research
- Protein structure and function studies
- Enhanced folding and solubility of target proteins
- Trapping soluble domains of proteins
- Trapping protein folding partners
- Identifying and engineering chaperones
- Protein-protein interaction studies
- Protein subcellular localization studies
- Protein quantification

Benefits:

- Simple system
- Does not require external reagents
- Provides sensitive analytical signal with pmol detection limits
- Enables experimentation both *in vivo* and *in vitro*
- Does not affect target protein function or folding
- Amenable to high-throughput assays

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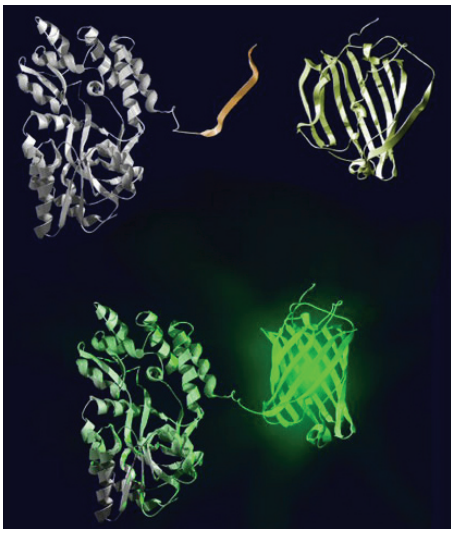
Summary:

Los Alamos National Laboratory (LANL) scientists have produced a portfolio of intellectual property related to expressed protein solubility and protein folding reporter inventions developed using Green Fluorescent Protein (GFP). The portfolio includes patented and patent-pending methods for applications that include expressed protein solubility folding research, protein quantification, protein subcellular localization, and protein structure/function studies. The LANL GFP portfolio provides researchers with a suite of tools for quick, sensitive protein folding, solubility and function studies.



Split-GFP fragments recombining to fluoresce.

A foundation piece of the portfolio is a method for directed evolution of proteins with enhanced folding and solubility properties. Using this method, LANL scientists have generated a "superfolder" GFP and a "superfolder" red fluorescent protein. Superfolder GFP folding is unaffected by the folding status of fusion partners, making it a robust reporter of protein expression, while increasing the range of proteins that can be successfully tagged with GFP. The directed evolution method may be used to enhance folding and solubility of other proteins of interest.

The Split-GFP Complementation System is useful in a wide range of protein expression applications, including *in vivo* expressed protein solubility, protein quantification and subcellular protein localization assays. Unlike other protein fragment complementation systems, Split-GFP complementation is spontaneous and does not require the use of fused heterologous interacting domains or external reagents. The set of Split-GFP fragments is also useful for measuring the success of directed evolution strategies and to assay for factors that either inhibit or promote protein folding and solubility (*Nature Biotech* 2005, 23: 102–107).

The third major piece of this portfolio is a protein folding reporter system that uses "insertion" vectors to sandwich test proteins between two domains of a reporter protein with an easily selected function. The reporter signal is activated only when target proteins fold correctly and are full length, eliminating false positives. This strategy has been successfully proven using both GFP and dihydrofolate reductase (DHFR) reporters. A set of GFP insertion reporters with "tunable" sensitivity to target protein folding greatly expands the versatility of the folding reporter system.

Development Stage: Proven technology

Patent Status: One issued patent and five patent applications; published documents available upon request. Foreign rights available for Split GFP and Insertion Vectors.

Licensing Status: Available for license, seeking partners for commercialization.

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